

Application No. 09/147,036
Reply to Office Action Dated March 24, 2004
Amendment Dated July 26, 2004

REMARKS

Claims 1-19, 41, and 43-59 were pending in the present application. Of these, claims 4-8 and 54 had been withdrawn from consideration by the Examiner. By this Amendment, Applicants have canceled claims 16, 17, and 18 without prejudice to Applicants' right to present the subject matter of these claims in a future continuation or divisional application. Applicants have amended the specification to include sequence identifiers into the figure descriptions in response to the Examiner's objection noted below. Applicants have amended claims 1, 3, 9-10, 14, 19, 41, 45, 55, 57, and 59 to address the Examiner's concerns. Support for the amendments can be found in the specification and claims as originally filed. Specifically, support for the amendments to claims 3, 41, 55, and 59 can be found, *inter alia*, at page 22, lines 4-8. Support for claim 14 can be found, *inter alia*, in original claim 14. Claims 1, 9, 10, 19, 45, and 57 have been amended for clarity. The present Amendment introduces no new matter and thus, its entry is respectfully requested. Upon entry of the present Amendment, claims 1-3, 9-15, 19, 41, 43-53, and 55-59 will be pending and under examination.

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Interview

Applicants acknowledge the telephonic Interview held March 4, 2004 between Examiner Ford and Applicants' undersigned attorney, Mr. Patrick Skacel, and make of record the following comments thereto. Consistent with the Examiner's Summary, Applicants acknowledge that Mr.

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Skacel and Examiner Ford discussed the fact that the present Office Action was originally mailed to an incorrect address. The Examiner kindly agreed that following Mr. Skacel's re-submission of a previously submitted Change of Address and Power of Attorney, the Examiner would re-mail the Office Action, with the new mailing date constituting the date from which the period for reply would be calculated. Applicants note that the new mailing date of the Office Action was March 24, 2004, and have calculated the period for reply from that date.

Rejections withdrawn

The Examiner withdrew all previous prior art rejections and the finality of the previous Office Action. In response, Applicants appreciate and acknowledge the withdrawal of these rejections.

Examiner's Objections to the Specification and claims

The Examiner stated that the specification fails to comply with the Sequence requirements by failing to include sequences identifiers for the sequences depicted in figures 6-24.

In response, Applicants have introduced appropriate sequence identifiers into the figure descriptions in the specification. Applicants believe that the introduction of these identifiers fully overcomes the Examiner's concerns.

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The Examiner also objected to the specification, asserting that all genus and species names of organisms appearing throughout the specification and claims are required to be underlined or italicized.

In response, Applicants have made appropriate changes to the claims, but have not undertaken the considerable burden of amending the numerous instances in the specification in which genus and species names appear. Applicants are aware of no requirement to do so. However, if there is such a requirement, Applicants respectfully request that the Examiner point out such requirement with reference to the relevant rule.

Examiner's Rejections under 35 U.S.C. § 112, first paragraph – enablement

The Examiner rejected claims 1-3, 9-19, 41, 43-53, and 55-59 under 35 U.S.C. §112, first paragraph, as lacking enablement. Specifically, the Examiner has indicated that a suitable biological deposit of “cell lines possessing the properties of a gram-negative host cell comprising a variant of the E.coli transporter domain of the AIDA protein” is required because it is not clear that such cell lines are known and publicly available or can be reproducibly isolated from nature without undue experimentation. According to the Examiner, without a publicly available deposit of the recited gram-negative host cell, one of ordinary skill could not be assured of the ability to practice the invention as claimed, because exact replication of the cell line is an unpredictable event.

In response, Applicants respectfully traverse the Examiner's rejection. It appears to Applicants that the Examiner is requiring a deposit of at least one cell line comprising a variant transporter, not merely a deposit of the preferred embodiment comprising the AIDA-I transporter. Applicants assert that the Examiner is incorrect in requiring any deposit, particularly one comprising a such a variant. Applicants point out that an Applicant need not guarantee that every aspect of the specification be precisely reproducible, but rather that the best mode and an adequate means of carrying out the invention be described. In this case, genetic material obtained from generally available sources is being inserted into a host cell that is also obtained from generally available sources, as the specification makes clear in various places, including pages 21, 33, and Figures 7-24. It is specifically noted at page 33 that the exemplary autotransporter sequence (AIDA-I) is available in data banks. The specification also sufficiently describes the use of variants, as indicated below. The gram-negative host bacteria recited in the claims therefore can be produced from known materials without undue experimentation, based on the description and teachings in the specification. Accordingly, no deposit of either a cell line comprising the preferred AIDA-I transporter domain, or a cell line comprising a variant is required to satisfy the enablement requirement.

The Examiner also rejected claims 1-3, 9-19, 41, 43-53, and 55-59 under 35 U.S.C. §112, first paragraph, as failing to enable one of skill in the art to practice the invention commensurate in scope with the claims. The Examiner has acknowledged that the specification is enabling for a process for presenting passenger peptides or polypeptides on the surface of gram-negative host

bacteria, wherein the transporter domain is an AIDA protein of *E. coli*, but has asserted, as above, that the specification does not reasonably provide enablement for processes in which the transporter domain is a variant of the AIDA protein of *E. coli*. Specifically, the Examiner has taken the position that the specification does not teach or define a structure for variants of the AIDA protein, and that there is no guidance as to which amino acids can be added, deleted, or substituted while retaining biological function.

In response, Applicants respectfully traverse this aspect of the rejection. The specification does in fact teach one of skill in the art how to modify the sequence of the AIDA-I protein to maintain biological function. See, for example, page 21, line 31, to page 22, line 8, describing variants produced by the modification of the sequence in the loop structures not involved in the membrane passage. Moreover, page 29 provides additional description. Accordingly, there is ample guidance in the specification to fully enable the claims. Nevertheless, without conceding the correctness of the Examiner's position, but to expedite allowance of the subject application, Applicants have amended claims 3, 41, 55, and 59, to recite that variants of the *E. coli* AIDA protein have a homology of at least 80% of the AIDA-1 autotransporter domain in at least their β -sheet regions. In view of these amendments, and the remarks set forth above, Applicants maintain that the claims as amended are fully enabled by the specification. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejections under 35 U.S.C. §112, first paragraph.

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Examiner's rejections under 35 U.S.C. §112, second paragraph

The Examiner also rejected claims 1-3, 9-19, 41, 43-53, and 55-59 under 35 U.S.C. §112, second paragraph, as failing to particularly point out and distinctly claim the subject matter that the Applicants regard as the invention. The Examiner has noted several examples and has listed them on pages 11 and 12 of the Office Action.

With respect to claim 1, the Examiner has indicated that the use of the term "step" is unclear. The Examiner has also indicated that claim 1's recitation of the term "under conditions" is not clear.

In response, Applicants have clarified claim 1 by removing the word "step" from the claim. With respect to the Examiner's assertion that "under conditions" is indefinite, Applicants respectfully traverse. One of ordinary skill in the art would clearly understand what is meant by this term as it is used in the claim. For instance, one of skill would know what conditions are commonly used to cultivate such bacteria to induce expression of the recited polynucleotide and presentation of the passenger peptide on the surface of the host bacterium. Moreover, the specification, at pages 29-30, notes, as general examples, the use of liquid culture or agar plates in such cultivation. Accordingly, claim 1, as amended, fully complies with 35 U.S.C. §112, second paragraph.

The Examiner has asserted that claims 9 and 10 recite "one or more peptides" of claim 1 without making clear to which such peptides these phrases refer.

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In response, Applicants have amended claims 9 and 10 to make more clear that the peptides to which these phrases refer are the passenger peptides (and polypeptides).

The Examiner has asserted that the recitation in claims 14 and 41 of “capable of” is unclear.

In response, Applicants have amended claim 14 for clarity. It now recites that the passenger polypeptide is the β chain of an MHC class II molecule comprising an N terminus to which amino acids for binding are attached. With respect to claim 41, it is unclear to Applicants precisely what the Examiner is objecting to, as it appears clear that “capable of” refers to the ability of the host bacteria to stably present the passenger protein on its surface. Applicants point out that claim 41 refers to a chimeric gene with a nucleotide sequence encoding a signal peptide, a passenger and a transporter domain. In contrast to claim 1, the protease recognition site is left out. If cleavage by protease is not possible, the passenger peptide remains bound to the cell surface after crossing the inner and the outer membrane of the host. Due to this property, bacteria displaying passengers with particular properties can be selected, as outlined in claim 41 (f) and (g). Therefore, the phrase “capable of stably presenting a passenger peptide or polypeptide on the cell surface” refers to the common mechanism of surface display known to the person skilled in the art (page 2, line 4, et seq.). Accordingly, claim 41 is clear as written and fully complies with the requirements of 35 U.S.C. §112, second paragraph. Applicants therefore respectfully request that the Examiner reconsider and withdraw its rejection.

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The Examiner indicated that claim 16 is unclear in its recitation of “variant passenger peptides” and “a mixture of non-variant passenger polypeptides.” Furthermore, the Examiner has rejected claim 18 based on its use of the phrase “comprising different transporter domains and different passenger proteins,” stating that it is unclear which different domains and proteins are referred to.

In response, without conceding the correctness of the Examiner’s position, but to expedite allowance of the subject application, Applicants have canceled claims 16, 17, and 18, without prejudice. Accordingly, this aspect of the Examiner’s rejection has been rendered moot.

The Examiner has indicated that claim 19’s recitation of “a library of variant peptides or polypeptides” is unclear.

In response, Applicants have amended claim 19 for clarity. Applicants point out that claim 15, from which claim 19 depends, refers to the expression and presentation of such libraries on the surface of the host bacterium, and claim 19 refers to selection of a single peptide or polypeptide from this library. Applicants point out to the Examiner that page 6, line 23 to page 7, line 20 of the specification refers, for example, to a process of expressing various polypeptides and selecting desired ones based on, *inter alia*, binding properties. Applicants assert that claim 19 as amended fully complies with the requirements of 35 U.S.C. §112, second paragraph. Applicants therefore respectfully request that the Examiner reconsider and withdraw its rejection.

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The Examiner has noted that claim 41 does not recite a step h), whereas claim 45, which depends from claim 41, refers to such a step.

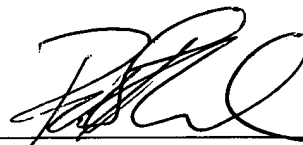
In response, Applicants have amended claim 45 to remove reference to a step h), thereby obviating the Examiner's rejection.

The Examiner noted that claims 55 and 57 refer to "steps" b) and e), which are not in fact method steps.

In response, Applicants have amended claims 55 and 57 to remove reference to any "steps," thereby obviating this aspect of the Examiner's rejection. Applicants maintain that all pending claims, as amended, are fully in compliance with 35 U.S.C. §112, second paragraph and respectfully request withdrawal of the rejections under this paragraph.

In view of the above remarks and amendments, Applicants believe that all of the Examiner's rejections and objections set forth in the March 24, 2004 Office Action have been fully overcome and that the present application is in condition for allowance. The Examiner is invited to telephone the undersigned if it is deemed to expedite allowance of the application.

Respectfully submitted,



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